

### ***Remarks***

Claims 65-124, 126, 127, 130-133 and 135-139 are pending in the captioned application. Claim 85 has been amended to correct a typographical error. Claims 65-84 and 130-133 have been canceled without prejudice or disclaimer. Applicants reserve the right to pursue the canceled subject matter in continuing applications. Claim 140 has been added. Support for this amendment can be found, for example, in paragraph 1 of page 9 of the instant specification. No new matter has been added by way of this amendment.

#### ***I. Rejection of the claims under 35 U.S.C. § 112, second paragraph***

Claims 65-84 and 130-133 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter. (Office Action, page 2.) Specifically, the Examiner maintains that claim 65 is indefinite since one of skill in the art cannot determine the metes and bounds of the term “substantially equal intensity,” and that unit of measure of “intensity” in claims 130-133 is unclear.

Applicants respectfully disagree with the Examiner however, to expedite prosecution, claims 65-84 and 130-133 have been canceled without prejudice or disclaimer. In view of this cancellation, the rejection of these claims under 35 U.S.C. § 112, second paragraph, is moot.

#### ***II. Rejection of claims under 35 U.S.C. § 102***

Claims 65-82, 85-101, 103, 105-121, 123, and 130-133 stand rejected under 35 U.S.C. § 102(b) as being anticipated by Carlson *et al.* (U.S. Patent No. 5,316,908). (Office Action, page 4.) Applicants respectfully disagree.

The Examiner asserts that Figure 1 of Carlson *et al.* discloses a nucleic acid ladder that meets the size, relative mass, and intensity requirements of claims 65-82, 85-100, 105-120, and 130-133. (Office Action, page 4.) Claims 65-82 and 130-133 have been canceled herein. Applicants have demonstrated in Figure 2 of the instant application that several commercially available nucleic acid ladders meet this size requirement. However, neither this figure or the other ladders disclosed in Figure 2, describe the relative mass requirements recited in the instant claims. Figure 1 merely lists a range of nucleic acid fragments, irrespective of the relative mass of each of those fragments.

The Examiner acknowledges that the present claims are directed to a nucleic acid ladder composition, and are not limited by an electrophoretic system or a requirement that the ladder be stained, or be allowed to fluoresce. (Office Action, page 4.) The Examiner goes on to assert that the properties of a composition do not impart patentability to the composition if the composition itself is old, and that the claims recite no chemical or physical component that would make the nucleic acid of the claims any different from the nucleic acid ladders of the prior art. However, Applicants assert that the present claims do recite a physical property that differentiates them from the prior art. Claim 85 recites that the relative mass (a physical property) of the nucleic acid fragments of each size is substantially equal. Claim 105 recites that the copy number (a physical property) of each fragment size is such that the total mass of each fragment size is substantially equal.

Carlson *et al.* fails to disclose this relationship amongst the nucleic acid fragments. Further, Carlson *et al.* alters the copy number of the largest and the smallest fragments in the ladder by increasing their copy number relative to the copy number of the middle range fragments (column 5, lines 55-63 of Carlson *et al.*). This alteration is described by Carlson *et al.* as one that overcomes the poor hybridization efficiency of the larger fragments and the poor retention of the smaller fragments on a membrane. If one were to increase the copy number of the larger fragments relative to the medium sized fragments (as described by Carlson *et al.*), both the relative mass and the total mass of the larger fragments would be increased in comparison to other fragments in the ladder. Because the claims prosecuted herein require that the relative mass (claims 85-104 and 140) or the total mass (claims 105-139) of each fragment in the ladder be substantially equal, Carlson *et al.* fails to disclose all of the limitations of these claims.

In view of the above, Applicants respectfully request that the Examiner reconsider and withdraw the rejection of the claims under 35 U.S.C. § 102(b).

The Examiner has further rejected 65-82, 85-101, 103, 105-121, 123, and 130-133 under 35 U.S.C. § 102(f) as not being invented by the inventor listed on the instant application. (Office Action, page 5.) The Examiner appears to be suggesting that the present claims were derived from Carlson *et al.* Applicants are confused as to this rejection because, as discussed above, the subject matter of the claims are not the same. Even if a rejection of the instant claims under 35 U.S.C. § 102(b) over Carlson *et al.* is proper as the Examiner asserts, it cannot be assumed that the present claims were derived from those of Carlson *et al.* "The mere fact that a claim recites

the use of various components, each of which can be argumentatively assumed to be old, does not provide a proper basis for a rejection under 35 U.S.C. § 102(f)." (*Ex parte Billottet*, 192 USPQ 413, 415 (Bd. App. 1976)). Derivation requires complete conception by another and communication of that conception by any means to the party charged with derivation prior to any date on which it can be shown that the one charged with derivation possessed knowledge of the invention. (*Kilbey v. Thiele*, 199 USPQ 290, 294 (Bd. Pat. Inter. 1978)). The Examiner has provided no evidence to suggest that the present claims were derived from another.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejection of the claims under 35 U.S.C. § 102(f).

### **III. Rejection of claims under 35 U.S.C. § 103**

Claims 102 and 122 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Carlson *et al.* in view of Schneeberger *et al.* (*PCR Methods and Applications* 4:234-238, (1995)). (Office Action, page 6.) Applicants respectfully disagree.

The Examiner asserts that one of skill in the art would have been motivated to have modified the nucleic acid ladder of Carlson *et al.* by staining with SYBR green as disclosed by Schneeberger *et al.* However, as discussed above, Carlson *et al.* does not teach or disclose a nucleic acid ladder comprising fragments that are substantially equal in relative mass or total mass. Schneeberger *et al.* fails to overcome this deficiency.

Claims 126, 127 and 135-139 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Carlson *et al.* (Office Action, page 7.) Applicants respectfully disagree.

The Examiner asserts that, while the prior art may not explicitly recite the mass relationships found in the rejected claims, such is deemed to be obvious in view of the prior art. (Office Action, page 7.) In support of this argument, the Examiner cites *In re Aller, Lacey, and Hall*, 105 USPQ 233 (CCPA 1955), and *KSR International Co. v. Teleflex Inc.*, 82 USPQ2d 1385 (U.S. 2007). However, each of these decisions relates to modifications that are within the technical grasp of one skilled in the art. Such has not been proven to be the case in the allegedly obvious modifications of Carlson *et al.* to arrive at the subject matter of the claims, as asserted by the Examiner.

In addition, as discussed above, the increase in copy number of the larger fragments compared to the medium-sized fragments would lead to an increase in the relative mass or the

total mass of the larger fragments, rather than a mass that is substantially equal as claimed herein. Furthermore, as evidenced by the multitude of commercially-available DNA ladders disclosed in Figure 2 of the specification that fail to meet this requirement, the need had not been met in the art. Thus, the Examiner has failed to provide a *prima facie* case of obviousness.

Claims 83, 84, 104, and 124 stand rejected under 35 U.S.C. § 103(a) as being unpatentable over Carlson *et al.* in view of Stanley (U.S. Patent No. 5,527,670) due to the use of bromophenol blue dye by Stanley. (Office Action, page 9.) Applicants respectfully disagree.

The Examiner asserts that one of skill in the art would have been motivated to have modified the nucleic acid ladder of Carlson *et al.* by staining with bromophenol blue as disclosed by Stanley. (Office Action, page 9.) However, as discussed above, Carlson *et al.* does not teach or disclose a nucleic acid ladder comprising fragments that are substantially equal in relative mass or total mass. Stanley fails to overcome this deficiency.

In view of the above, Applicants respectfully request reconsideration and withdrawal of the rejections of the claims under 35 U.S.C. § 103(a).

***Conclusion***

Applicants believe that a full and complete reply has been made to the outstanding Office Action and, as such, the present application is in condition for allowance. If the Examiner believes, for any reason, that personal communication will expedite prosecution of this application, the Examiner is invited to telephone the undersigned at the number provided.

Prompt and favorable consideration of this Amendment and Reply is respectfully requested.

Respectfully submitted,

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